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# THE UNITED STATES OF AMERICA

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**June 07, 2004**

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**APPLICATION NUMBER:** ***60/517,073***
**FILING DATE:** ***November 05, 2003***

**PRIORITY DOCUMENT**
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**Certifying Officer**

PATENT APPLICATION SERIAL NO. _____

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE
FEE RECORD SHEET

11/06/2003 HVUONG1 00000122 60517073
01 FC:2005 80.00 OP

PTO-1556
(5/87)

*U.S. Government Printing Office: 2002 — 489-267/69033

PTO/SB/16 (08-03)
Approved for use through 07/31/2006. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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# PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

Express Mail Label No.

| INVENTOR(S) | | |
|---|---|---|
| Given Name (first and middle [if any]) | Family Name or Surname | Residence (City and either State or Foreign Country) |
| MORDECHAI | DEUTSCH | MOSHAV OLESH, ISRAEL |

*Additional inventors are being named on the* _____ *separately numbered sheets attached hereto*

**TITLE OF THE INVENTION (500 characters max)**

A MICROSAMPLE CELL EXTRACTION TOUCHING METHOD

*Direct all correspondence to:* **CORRESPONDENCE ADDRESS**

☐ Customer Number:

OR

| | | | | | |
|---|---|---|---|---|---|
| ☑ Firm or Individual Name | SCHOTTENSTEIN CELLOME RESEARCH CENTER | | | | |
| Address | BAR ILAN UNIVERSITY | | | | |
| Address | | | | | |
| City | RAMAT GAN | State | | Zip | 52900 |
| Country | ISRAEL | Telephone | 5342675 | Fax | +97235342019 |

U.S. PTO 60/517073 10503 2258

**ENCLOSED APPLICATION PARTS (check all that apply)**

☑ Specification *Number of Pages* 5
☑ Drawing(s) *Number of Sheets* 2
☐ Application Data Sheet. See 37 CFR 1.76
☐ CD(s), Number _____
☐ Other (specify) _____

**METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT**

☑ Applicant claims small entity status. See 37 CFR 1.27.
☑ A check or money order is enclosed to cover the filing fees.
☐ The Director is herby authorized to charge filing fees or credit any overpayment to Deposit Account Number: _____
☐ Payment by credit card. Form PTO-2038 is attached.

FILING FEE Amount ($): 80

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

☐ No.
☑ Yes, the name of the U.S. Government agency and the Government contract number are: US ARMY MEDICAL RESEARCH AQUISITION ACTIVITY AWARD# DAMD 17-01-1-0131



*Respectfully submitted,*

SIGNATURE _____ Date 11-05-2003

TYPED or PRINTED NAME MORDECHAI DEUTSCH REGISTRATION NO. _____ *(if appropriate)*

TELEPHONE +97235344675 Docket Number: 27

***USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT***

13281 U.S.PTO 110503

PTO/SB/17 (10-03)
Approved for use through 07/31/2006. OMB 0651-0032
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# FEE TRANSMITTAL for FY 2004

*Effective 10/01/2003. Patent fees are subject to annual revision.*

[X] Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 80

| Complete If Known | |
|---|---|
| Application Number | |
| Filing Date | 11/05/2003 |
| First Named Inventor | MORDECHAI DEUTSCH |
| Examiner Name | |
| Art Unit | |
| Attorney Docket No. | 27 |

## METHOD OF PAYMENT (check all that apply)

[X] Check [ ] Credit card [ ] Money Order [ ] Other [ ] None

[ ] Deposit Account:

Deposit Account Number
Deposit Account Name

The Director is authorized to: (check all that apply)

[ ] Charge fee(s) indicated below [ ] Credit any overpayments

[ ] Charge any additional fee(s) or any underpayment of fee(s)

[ ] Charge fee(s) indicated below, except for the filing fee to the above-identified deposit account.

## FEE CALCULATION

### 1. BASIC FILING FEE

| Large Entity Fee Code | Large Entity Fee ($) | Small Entity Fee Code | Small Entity Fee ($) | Fee Description | Fee Paid |
|---|---|---|---|---|---|
| 1001 | 770 | 2001 | 385 | Utility filing fee | |
| 1002 | 340 | 2002 | 170 | Design filing fee | |
| 1003 | 530 | 2003 | 265 | Plant filing fee | |
| 1004 | 770 | 2004 | 385 | Reissue filing fee | |
| 1005 | 160 | 2005 | 80 | Provisional filing fee | 80 |

SUBTOTAL (1) ($) 80

### 2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

| | Extra Claims | | Fee from below | Fee Paid |
|---|---|---|---|---|
| Total Claims | -20** = | X | | = |
| Independent Claims | -3** = | X | | = |
| Multiple Dependent | | | | = |

| Large Entity Fee Code | Large Entity Fee ($) | Small Entity Fee Code | Small Entity Fee ($) | Fee Description |
|---|---|---|---|---|
| 1202 | 18 | 2202 | 9 | Claims in excess of 20 |
| 1201 | 86 | 2201 | 43 | Independent claims in excess of 3 |
| 1203 | 290 | 2203 | 145 | Multiple dependent claim, if not paid |
| 1204 | 86 | 2204 | 43 | ** Reissue independent claims over original patent |
| 1205 | 18 | 2205 | 9 | ** Reissue claims in excess of 20 and over original patent |

SUBTOTAL (2) ($)

**or number previously paid, if greater; For Reissues, see above

## FEE CALCULATION (continued)

### 3. ADDITIONAL FEES

| Large Entity Fee Code | Large Entity Fee ($) | Small Entity Fee Code | Small Entity Fee ($) | Fee Description | Fee Paid |
|---|---|---|---|---|---|
| 1051 | 130 | 2051 | 65 | Surcharge - late filing fee or oath | |
| 1052 | 50 | 2052 | 25 | Surcharge - late provisional filing fee or cover sheet | |
| 1053 | 130 | 1053 | 130 | Non-English specification | |
| 1812 | 2,520 | 1812 | 2,520 | For filing a request for *ex parte* reexamination | |
| 1804 | 920* | 1804 | 920* | Requesting publication of SIR prior to Examiner action | |
| 1805 | 1,840* | 1805 | 1,840* | Requesting publication of SIR after Examiner action | |
| 1251 | 110 | 2251 | 55 | Extension for reply within first month | |
| 1252 | 420 | 2252 | 210 | Extension for reply within second month | |
| 1253 | 950 | 2253 | 475 | Extension for reply within third month | |
| 1254 | 1,480 | 2254 | 740 | Extension for reply within fourth month | |
| 1255 | 2,010 | 2255 | 1,005 | Extension for reply within fifth month | |
| 1401 | 330 | 2401 | 165 | Notice of Appeal | |
| 1402 | 330 | 2402 | 165 | Filing a brief in support of an appeal | |
| 1403 | 290 | 2403 | 145 | Request for oral hearing | |
| 1451 | 1,510 | 1451 | 1,510 | Petition to institute a public use proceeding | |
| 1452 | 110 | 2452 | 55 | Petition to revive - unavoidable | |
| 1453 | 1,330 | 2453 | 665 | Petition to revive - unintentional | |
| 1501 | 1,330 | 2501 | 665 | Utility issue fee (or reissue) | |
| 1502 | 480 | 2502 | 240 | Design issue fee | |
| 1503 | 640 | 2503 | 320 | Plant issue fee | |
| 1460 | 130 | 1460 | 130 | Petitions to the Commissioner | |
| 1807 | 50 | 1807 | 50 | Processing fee under 37 CFR 1.17(q) | |
| 1806 | 180 | 1806 | 180 | Submission of Information Disclosure Stmt | |
| 8021 | 40 | 8021 | 40 | Recording each patent assignment per property (times number of properties) | |
| 1809 | 770 | 2809 | 385 | Filing a submission after final rejection (37 CFR 1.129(a)) | |
| 1810 | 770 | 2810 | 385 | For each additional invention to be examined (37 CFR 1.129(b)) | |
| 1801 | 770 | 2801 | 385 | Request for Continued Examination (RCE) | |
| 1802 | 900 | 1802 | 900 | Request for expedited examination of a design application | |

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid SUBTOTAL (3) ($)

| SUBMITTED BY | | | | (Complete if applicable) | |
|---|---|---|---|---|---|
| Name (Print/Type) | DR. Roberts VASL | Registration No. (Attorney/Agent) | | Telephone | +972534466 75 |
| Signature | Vasl | | | Date | 11/5/03 |

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This collection of information is required by 37 CFR 1.17 and 1.27. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

*If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.*

PROVISIONAL PATENT APPLICATION

Inventors: MORDECHAI DEUTSCH

Title: A MICROSAMPLE CELL EXTRACTION TOUCHING METHOD

## FIELD AND BACKGROUND OF THE INVENTION

The present invention relates to cellomics and, more particularly, to a method employing a collection system for live cells from a tissue with a minimal amount of damage to the tissue.

Tissue specimens for pathological analysis are obtained for histological and pathological observation in order to determine factors such as the characteristic features of the tissue. For the purpose of diagnosis it may be highly advantageous to carry out functional assays on living cells that should be obtained before fixation. This functional assay can only be performed if the cellular extraction will cause minimal damage to the tissue structure under study.

A ubiquitous method used by pathologists employs fixation of thin cuts of tissue with the use of formalin for example. However as stated above, this fixation procedure kills the cells being studied and thus render them useless for functional analysis.

All tissues are open to circulating fluxes of various cells of the immune system. The level and components of this circulation is specifically sensitive to various pathological situations. Functional studies therefore may be instrumental for diagnostic purposes and therefore there is a growing need to extract such cells with a minimal damage to the tissue before regular pathological procedures.

## BRIEF DESCRIPTION OF THE DRAWING

The invention is herein described, by way of example only, with reference to the accompanying drawing. With specific reference now to the drawing in detail, it is stressed that the particulars shown are by way of example and for purposes of illustrative discussion of the preferred embodiments of the present invention only, and are presented in the cause of providing what is believed to be the most useful and readily understood description of the principles and conceptual aspects of the invention. In this regard, no attempt is made to show structural details of the invention in more detail than is necessary for a fundamental understanding of the invention, the description taken with the drawings making apparent to those skilled in the art how the several forms of the invention may be embodied in practice.

Figure 1

## DESCRIPTION OF THE PREFERRED EMBODIMENTS

Before explaining at least one embodiment of the invention in detail, it is to be understood that the invention is not limited in its application to the details of construction and the arrangement of the components set forth in the following description or illustrated in the drawings. The invention is capable of other embodiments or of being practiced or carried out in various ways. Also, it is to be understood that the phraseology and terminology employed herein is for the purpose of description and should not be regarded as limiting.

Cells may be observed and/or manipulated in numerous settings known in the art. One example of such a setting is a cell chip (ITICBP assembly) as described by Deutsch in PCT patent application number WO 03/035824 filed 25 October 2001 which enables the observation and manipulation of single cells or a defined amount of cells in their own individual locations.

In the closed ITICBP assembly described in the previous report, only cells in suspension can be loaded. In order to allow loading by 'touch', a direct attachment between the tissue and the ITICBP surface may be performed, while the latter is situated in the cellchip housing/holder. In order to enable a 'touch', a removeable ITICBP sealing cover glass is included in the ITICBP which does not exist in the

former ITICBP as described by Deutsch in PCT patent application number WO 03/035824.

The ITICBP is situated and held in a rubber socket. External pressure exerted on a cover glass on top of the socket, creates a sealed measurement micro liter volume compartment. The rubber socket contains micro channels/pipes, which permit the transfer of cell suspension, in addition to solutions to the cells held in the cellchip.

At this stage, the system channels may be tested by the injection of solution via the micro channels by using needles for example. According to preferred embodiments of the invention a cell chip is made with a removable glass or plastic top. Preferably when the cover is on, the system may be tested for any leaks by flushing the system with a solution. The cover may then be removed and then in order to ensure that there is no air in the system more solution may be added to the system or the solution may be moved backward to the direction that it was introduced as described above such that a droplet may be formed on top of the grid and visible as is seen in figure 1. Now it is ready for touch. The tissue to be studied is laid (touched) on top of the open grid for a short period of time of up to a number of minutes. During this period cells which have been freed by the fresh cutting of the tissue may settle down onto the grid. This freeing of cells and their settling down into the wells may be facilitated by gently splashing the tissue surface adjacent to the wells with solution which may be injected/pumped via the inlet syringe. The tissue is then gently removed from the chip and then the cover glass may then be returned and closed preferably hermetically while preferably refraining from bubble creation.

The cell-laden system may now be exposed to reagents and other fluorescent probes for manipulations and observation.

A typical cell-chip in which each well may be hexagonally shaped will be described here as an example of a cell-chip. This is a dense configuration of wells. Wells that may be fashioned from a rigid source such as glass or a plastic may be surrounded by very sharp tips as shown in figure 2. In performing that procedure, the loaded cells may become damaged (injured) due to the very sharp tips of the 6 columns surrounding each well.

According to further embodiments of the present invention, the problem of cell damage due to sharp tips surrounding the wells may be solved by dulling the well

tips, as can be seen in Fig. 3. Another solution to this problem would be to fashion the wells from a compliant material such as a gel.

Although the invention has been described in conjunction with specific embodiments thereof, it is evident that many alternatives, modifications and variations will be apparent to those skilled in the art. Accordingly, it is intended to embrace all such alternatives, modifications and variations that fall within the spirit and broad scope of the present specification.

WHAT IS CLAIMED:

1. A method and a system for delivering live cells from a tissue to a cell-chip essentially as described hereinabove or depicted in the figures.

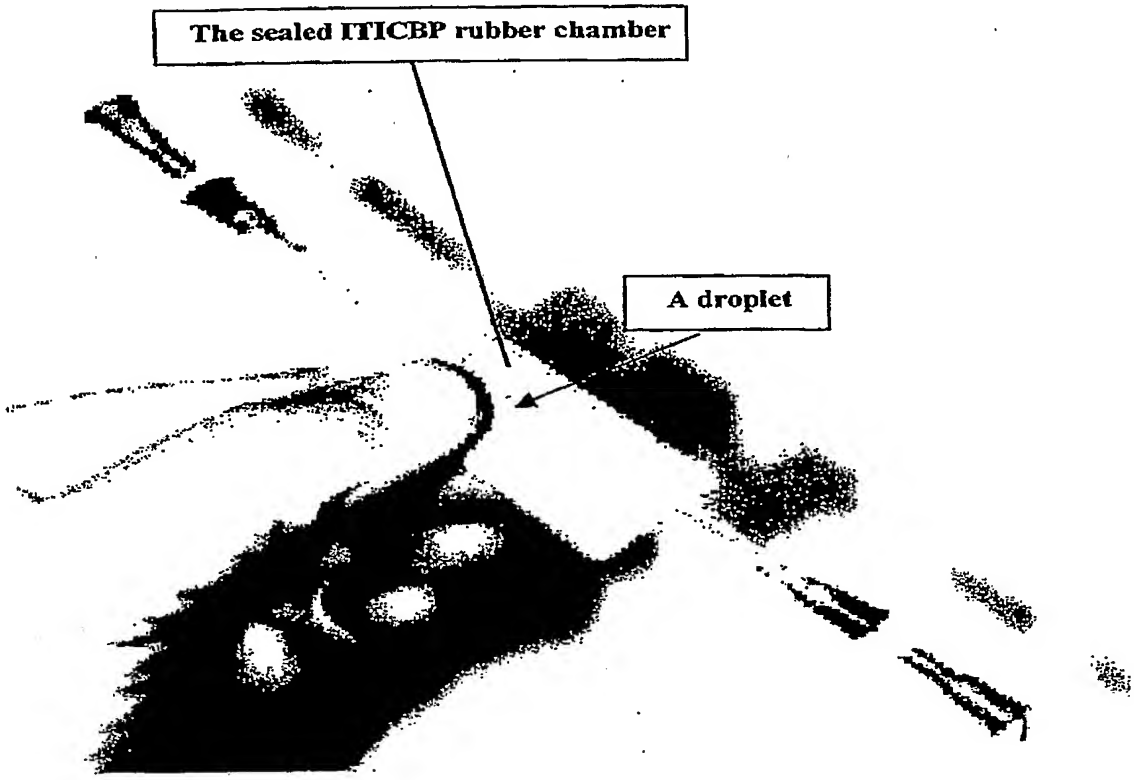
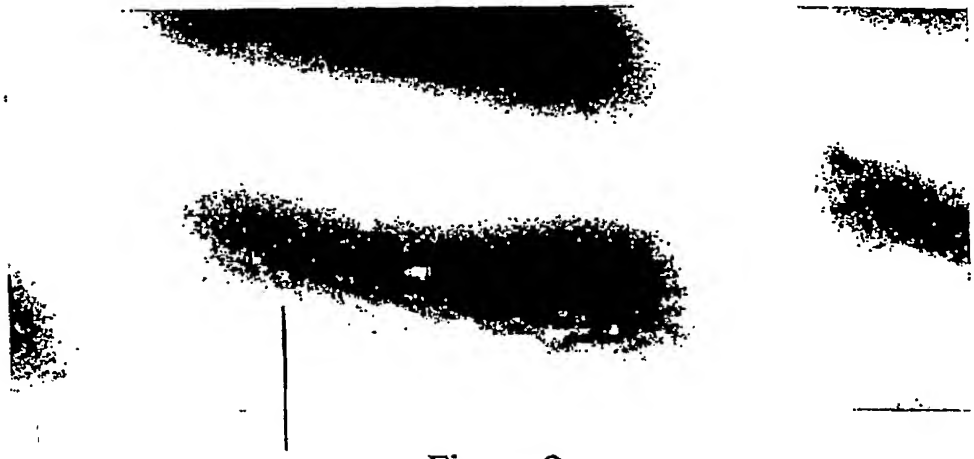



Figure 1



sharp tips

Figure 2


dull tips

Figure 3